Remarks

Claims 24-33 and 48-57 are pending. Claims 1-23 and 34-47 are canceled. Applicants reserve the right to pursue the subject matter of all canceled claims in one or more continuation or divisional applications.

Rejections under 35 U.S.C. § 101, first paragraph

Claims 24-33 and 48-57 have been rejected under 35 U.S.C. § 101. *See* Paper No. 0605, page 2, 6th paragraph. Applicants respectfully disagree and traverse.

More particularly, with regard to Exhibits A-D submitted with Applicant's previous response of April 5, 2005, the Examiner states that Applicants have "...failed to demonstrate any sequence similarity or structural similarity between SEQ ID NO:145 and any proteins...known in the art at the time of filing." *See* Paper No. 0605, page 3, 2nd paragraph. Applicants respectfully submit that Exhibits A-D were submitted not because they disclose polypeptides homologous to the claimed polypeptides, but because they show, prior to the effective priority date of the present invention, the well-established use of polypeptides, like the claimed polypeptides, with tissue and/or cancer specific expression patterns, as molecular markers for the diagnosis of particular types of cancers. *See* for example, Rajkumar *et al.* which describe the use of albumin to diagnose primary hepatocellular carcinoma. Accordingly, Applicants respectfully request reconsideration of these publications on this basis (as initially requested in Applicants' Response filed April 5, 2005, page 3, third paragraph).

The Examiner further alleges that disclosure of an expression pattern is not the same as disclosing the activity of a polypeptide, "[a]n activity is something the protein does in the cell in which [it is] expressed. Catalyzing an enzymatic reaction is one example. The specification, as filed, fails to identify any activity for the claimed polypeptides." *See* Paper No. 0605, page 3, 3rd paragraph. Applicants respectfully disagree. Nevertheless, even assuming *arguendo*, that the present specification does not disclose an activity (as defined by the Examiner) for the claimed polypeptides, Applicants respectfully submit that the claimed polypeptides can still have patentable utility under 35 U.S.C. § 101.

Indeed, an analogous situation occurs in the chemical arts where a composition that does not, *per se*, have patentable utility, can have patentable utility if it is useful as a chemical intermediate in a reaction to create a product which is patentably useful. *See In re Joly,* 376 F.2d 906, 908 (CCPA 1967) and *In re Kirk*, 376 F.2d 936 (C.C.P.A. 1967). In the present situation, the claimed polypeptides can be used to generate or select polypeptide specific antibodies which can be used to diagnose hepatoma or hepatoblastoma. Therefore, because antibodies (the product) that bind the claimed polypeptides have a specific, substantial and credible utility, *i.e.*, as a diagnostic for liver cancer, the polypeptides (the chemical intermediate) used to generate or select these antibodies also have a specific, substantial and credible utility.

The Examiner further states that,

> Applicant questions which aspect of the asserted utilities fail to meet the standard...the polypeptide of SEQ ID NO:145 does not have a specific, substantial and credible utility, and does not have a well-established utility according to 35 U.S.C. § 101
>
> Applicant argues the expression pattern of the claimed polypeptide in a given tissue alone supports the asserted utility of diagnosis, detection, prevention and/or treatment of liver disorders. This is not persuasive, as the specification fails to provide any evidence that SEQ ID NO:145 is related to any disorder of the liver.

See Paper No. 0605, page 3, paragraphs 4 and 5. With these statements the Examiner appears to be alleging that Applicants asserted utility is not specific or substantial because it lacks credibility. Applicants respectfully disagree.

With regard to the issue of credibility, the M.P.E.P. utility guidelines instruct:

> Office personnel are reminded that they must treat as true a statement of fact made by an applicant in relation to an asserted utility, unless countervailing evidence can be provided that shows that one of ordinary skill in the art would have a legitimate basis to doubt the credibility of such a statement.

See, M.P.E.P. (8th Ed., Rev. May 2004), § 2107 (II)(D), second paragraph. Applicants respectfully submit that the Examiner has not provided countervailing evidence showing that one of ordinary skill in the art would judge the specification as failing to,

"...provide any evidence that SEQ ID NO:145 is related to any disorder of the liver." *Id.* To the contrary, Applicants respectfully submit that upon considering that the claimed polypeptides are expressed primarily in liver, to a lesser extent in testis, and also in hepatocellular tumor, re-excision, one of ordinary skill in the art would more likely than not believe that antibodies against the claimed polypeptide could be used, for example, to diagnose hepatoma or hepatoblastoma[1]. More particularly, as explained in Applicants previous response of April 5, 2005, one of ordinary skill in the art would recognize that antibodies against the claimed polypeptide can be used to determine if a cancerous growth in the liver began in the liver itself, *i.e.,* as a hepatoma or hepatoblastoma, or originated elsewhere in the body and metastasized to the liver (a common challenge for human pathologists).

With regard to the post-filing date art of Smith, *et al.*, and Rouault, *et al.*, (submitted as Exhibits E and F with Applicants' previous response), the Examiner states that, "...these publications set forth experiments, data and procedures that go beyond those described in the specification. The specification does not set forth the experiments of Smith, or [Rouault] that led to their conclusions."

Applicants respectfully remind the Examiner that post-filing date art is considered to corroborate an asserted utility insofar as it, "...substantiate[s] any doubts as to the asserted utility since this [it] pertains to the accuracy of a statement already in the specification." *In re Marzocchi*, 439 F.2d 220, 169 USPQ 367 (CCPA 1971). Some of the experiments of Smith, *et al.*[2], and Rouault, *et al.*[3], do just that by confirming the teachings of the present specification that the HFVAB79 polypeptide is expressed primarily in liver tissue, and also in hepatocellular tumor, re-excision.

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[1] As stated on page 29, paragraph 78, first 3 sentences of the present specification (emphasis added): The tissue distribution in liver tissue indicates that polynucleotides and polypeptides corresponding to this gene would be useful for the diagnosis, detection, prevention and/or treatment of liver disorders, particularly those affecting the immune and hematopoietic systems, including hepatomas. Representative uses are described in the "Hyperproliferative Disorders," "Infectious Disease," and "Binding Activity" sections below, in Example 11, and 27, and elsewhere herein. Briefly, polynucleotides and/or polypeptides corresponding to this gene can be used for the detection, treatment, and/or prevention of hepatoblastoma, jaundice, hepatitis, or liver metabolic diseases and conditions that are attributable to the differentiation of hepatocyte progenitor cells.

[2] *See* Smith *et al.*., page 862, Fig. 3 and page 863, left column, lines 9-13, which reads "However, the most interesting of the identified potential serological markers was PLA2G13. This gene was up-regulated in 16 of 20 HCC tumors, and the least up-regulated in the cirrhotic liver relative to normal liver (Fig. 2B)." (emphasis added)

[3] *See* Rouault *et al.*, page 11500, Fig. 5.

Therefore, these post-filing date references corroborate Applicants' assertion that the claimed polypeptides can be used to generate or select antibodies that could be useful in the diagnosis of liver cancer, irregardless of whether or not they set forth additional, "experiments, data and procedures that go beyond those described in the specification." *Id.*

The Examiner further states that, "[a]pplicant argues that polypeptides can be used to generate antibodies that may have a further use. This is not persuasive. Further research utility is not deemed to meet the standard of specific, substantial and credible. There is no disclosed or real world utility associated with the claimed protein. Further experimentation is necessary to attribute a utility to the claimed protein." *See* Paper No. 0605, page 4, first paragraph. Applicants respectfully disagree.

As described above, antibodies generated or selected using the polypeptides of the present invention meet the requirement for utility under 35 U.S.C. § 101, and the polypeptides used to generate or select these antibodies have patentable utility, even if the reactions they catalyze, *e.g.,* what the polypeptide binds to and/or the substrate it modifies, is unknown. Applicants have thus shown that one of ordinary skill in the art would not reasonably doubt that the claimed invention has a credible, specific and substantial utility. Accordingly, Applicants respectfully request that rejection of claims 24-33 and 48-57 under 35 U.S.C. § 101 be reconsidered and withdrawn.

With regard to the remainder of the Examiner's 35 U.S.C. § 101 rejection, from page 3, 3rd paragraph to page 5, 3rd paragraph, Applicants note that this is substantially identical to the rejections given in the Office Actions dated June 29, 2004 (*See* page 3, second paragraph to page 4, 3rd paragraph) and February 9, 2005 (*See* page 3, 3rd paragraph to page 4, 3rd paragraph). As Applicants answered each aspect of the 35 U.S.C. § 101 rejection put forth in the Office Action of June 29, 2004 in the response submitted September 28, 2004, Applicants respectfully request that the Examiner reconsider the response submitted September 28, 2004.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 24-33 and 48-57 have been rejected under 35 U.S.C. § 112, first

paragraph because the claimed invention is allegedly "...not...supported by a specific, substantial, and credible utility...one skilled in the art clearly would not know how to use the claimed invention." *See* Paper No. 0605, page 5, 4th paragraph.

Applicants respectfully disagree and traverse. The Examiner "should not impose a 35 U.S.C. § 112, first paragraph, rejection grounded on a 'lack of utility' basis unless a 35 U.S.C. §101 rejection is proper." M.P.E.P. § 2107 (IV) at 2100-36. As explained above, claims 24-33 and 48-57 comply with the utility requirement of 35 U.S.C. § 101. Accordingly, Applicants respectfully request that rejection of claims 24-33 and 48-57 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

Conclusion

Applicants respectfully request that the above-made remarks be entered and made of record in the file history of the instant application. The Examiner is invited to call the undersigned at the phone number provided below if any further action by Applicants would expedite the examination of this application. Alternatively, if the Examiner believes that an interview would help resolve any remaining issues, Applicants urge the Examiner to call the undersigned to arrange an interview at their earliest convenience. If there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136 that is not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Dated: 9/20/2005

Respectfully submitted,

By _____

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